REMARKS

This is in response to the Office Action that was mailed on April 8, 2005. Applicants are shocked by the Examiner's indication that claims 1, 2, 6-8, 13, 14, 19, 25-27, and 29 are no longer allowed. Applicants gratefully acknowledge the indicated allowability of claims 25-27. New claims 30-32 are added, directed to the peptides of SEQ ID NO:29, SEQ ID NO:31, and SEQ ID NO:32, respectively. No new matter is introduced by this Amendment. Claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23, and 25-32 are pending in the application.

Election Of Species

Claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23, and 25-29 all ***read on or relate to the elected species***. The outstanding Office Action states that claims 10, 15, 16, 20, and 23 are withdrawn from consideration. In response to an election of species, Applicants had elected the species of invention that involves SEQ ID NO:30, recited in claim 25. Claim 25 depends from claim 10 – in other words, ***claim 10 and claims 15, 16, 20, and 23 dependent thereon include the elected species***. It is respectfully submitted that the Examiner is not justified in withdrawing these claims from consideration.

Written Description – first rejection

Claims 22 and 28 were rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement. Office Action, pages 3-5.

The Examiner alleges that: "there is no written description for ... **preventing or treating a subject** for the conditions being claimed (i.e., preventing or treating primary tumor growth or metastasis)". Office Action, page 4, middle (emphasis in original). Typical of the claims in question is

claim 23 (which is identical to claims 22 and 28, except for its dependence on claim 15 rather than on claim 13 or on claim 26):

> 23. A method for preventing or treating primary tumor growth or metastasis by inhibiting tumor angiogenesis, said method comprising administering the composition of claim 15 to a subject presenting a tumor.

The claims in question do not recite that tumors are being prevented (nor do they recite that a subject is being prevented). Instead, the claims recite (in part) that the ***growth or metastasis*** of tumors that already exist in a subject ("a subject presenting a tumor") is treated or prevented. Thus the invention in question involves (among other things) preventing tumor growth or metastasis.

The specification contains ample written description of this invention. For instance, "effective doses of the peptides of the present invention will be about 0.2 μg/kg/day to about 2 mg/kg/day for inhibition of ***metastasis***. ... the dosage ranges will be about 10-fold higher for inhibition of primary tumor ***growth***." Specification, page 8, lines 6-11.

The Examiner asserts that: "... there is no written description for *in vivo* showing for the effectiveness of the peptides as claimed not there is a recognized model (identified as useful)". Office Action, page 4, middle. Example 4 at page 12 of the present specification constitutes an *in vivo* showing for the effectiveness of the peptides as claimed. In any event, ***proving effectiveness is not a consideration in a rejection on the ground of failure to meet the written description requirement.***

The Examiner argues that "Applicant's claims are directed to prevention, and there is no objective factual evidence in the specification or references enclosed or cited by Applicant to show that prevention has occurred since no adequate time was given to mimic the protocol administered in the animal models and allow evaluation of active immune response". First, this line of reasoning seems to

imply that Applicants have not ***proved*** in the specification that their invention functions in the manner that they say that it works in. While such considerations might be relevant to a rejection for failing to comply with the enablement requirement of the first paragraph of 35 U.S.C. §112, they are totally irrelevant to the present rejection (written description). Second, the present invention is thought to work through inhibition of angiogenesis, starving the tumor cells for nutrients and oxygen. The relevance of an immune response in the present invention is not apparent to Applicants' representative.

It is clear that the inventions of each of claims 22, 23, and 28 are fully described – in writing – in the specification. Withdrawal of the rejection of record is respectfully solicited.

Written Description – second rejection

Claims 1, 2, 6-8, 13, 14, 19, 22, and 29 were rejected under the first paragraph of 35 U.S.C. §112 as allegedly failing to comply with the written description requirement. Office Action, pages 5-10. It is not immediately apparent why claim 22 is rejected on this ground twice.

The Examiner argues that "There is no description in the instant specification for the claimed peptide". The Examiner alleges that "No reference sequence has been provided". The Examiner argues that "There is no written description indicating the claimed variants for the peptide". The Examiner states – incomprehensibly – that "The use of 7-20 amino acid residues with any peptide comprising a portion of an endostatin protein suggests that the amino acid sequence/residue intended to be modified by substitution is either is not know or Applicant contemplates modification of a portion of an endostatin protein by substitution form 0 to 20 of amino acid residues in the peptide. Thus, the scope of the claims is not commensurate with the written description".

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why ***persons skilled in the art*** would not recognize in the disclosure a description of the invention defined by the claims") (emphasis supplied).

Endostatin is a well known polypeptide of 184 amino acids. In addition to its biological recitations, claim 1 herein recites a peptide that comprises "a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide". There are only a finite number of 7-amino acid portions of the endostatin peptide, even fewer 8-amino acid portions, and fewer yet of the larger portions up to the 20-amino acid portions. A ***person skilled in the art***, upon reading the present specification, could readily envision the list of all the recited 7-20 amino acid "portions" of endostatin. That list would, of course, contain far more peptides than are covered by claim 1. A ***person skilled in the art,*** having read the specification, would learn what portion of the endostatin polypeptide should be obtained and would readily envision how to eliminate from the 'all 7-20 amino acid portions' list those portions that did not contain a pair of proline residues, at least one of which is at or penultimate to a terminus of the peptide "portion" of the 184 amino acid endostatin sequence. These two manipulations of the endostatin sequence, each of which is within the expected skill of the art, would leave the small group of proline-pair peptides that represent structures within claim 1.

To determine operability of any one of those structures, the ***person skilled in the art*** would then run tests that are described in the present specification on each of the peptides in the small group of proline-pair peptides that had been derived from the endostatin sequence in order to determine whether

each peptide exhibits an IC_{50} of 20 μM or less in a bovine aorta endothelial cell proliferation assay or exhibits inhibition of angiogenesis in a chick chorioallantoic membrane assay of at least 30% at a dose of 50 μg/coverslip. These steps – which once conceived and described as in the present specification are technologically simple – would identify each and every peptide covered by claim 1.

Applicants respectfully maintain that there is nothing in the steps discussed above that is beyond the expected skill of those persons to whom the present disclosure is directed. In other words, Applicants believe that the present disclosure provides ***persons skilled in the art*** with a written description of the claimed invention.

It has been demonstrated that the inventions of each of claims 1, 2, 6-8, 13, 14, 19, 22, and 29 is fully described – in writing – in the specification. The Examiner is reminded, however, that the Examiner – not Applicant – has the burden of proof with respect to failure to meet the written description requirement. See *In re Wertheim, supra.* An analysis is needed from the Examiner explaining why the structural definition and the functions set forth in claim 1 do not adequately identify the claimed genus of peptides. Withdrawal of the rejection of record is respectfully solicited.

Conclusion

If there are any remaining issues or questions, the Examiner is invited to telephone Richard Gallagher (Reg. No. 28,781) at (703) 205-8008.

If necessary, the Commissioner is hereby authorized to debit Deposit Account No. 02-2448 for any additional fee required under 37 C.F.R. §1.16 or §1.17, particularly extension of time fees.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

By _____

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